



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,647	11/27/2001	Bernd Riedl	BAYER 18A	1010
23599 7590 09/24/2007 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			EXAMINER RAO, DEEPAK R	
			ART UNIT 1624	PAPER NUMBER
			MAIL DATE 09/24/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

09/993,647

Applicant(s)

RIEDL ET AL.

Examiner

Deepak Rao

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 74,81,87,93,99-104,106-115 and 117-119 ~~is~~ are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 74,81,87,93,99-104,106-115 and 117-119 ~~is~~ are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>20070511, 20070529 &amp; 20070629</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 29, 2007 has been entered.

Claims 74, 81, 87, 93, 99-115 and 117-119 are pending in this application.

### ***Withdrawn Rejections/Objections:***

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

### ***The following rejections are maintained:***

1. Claims 74, 81, 87, 93, 99-103, 106-114 and 117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of carcinoma of the colon (based on the *in vitro* treatment of the tumor cell lines HCT116 and DLD-1 provided in the specification), does not reasonably provide enablement for a method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas; or a method for inhibiting RAF-kinase in a human or mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the

Art Unit: 1624

invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Applicant cites *In re Marzocchi*, 169 USPQ 367, and argues that ‘there is no evidence that the claimed methods are not enabled’. However, the examiner has provided both reasoning including the nature of the invention, which is directed to an unpredictable art, citation of case law as well as relevant publication to support the reason for the rejection. Applicant has not identified any state of the art references that clearly establish correlation between the assays employed in the specification and clinical efficacy for the treatment of the claimed diseases. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of *in vivo* efficacy by those skilled in the art. Applicant’s specification would not have enabled a person of ordinary skill in the art to use the full scope of the claimed invention. The breadth is not commensurate in scope with the claims, i.e., ‘methods for treating solid tumor, carcinoma, myeloid disorder or adenoma’ or method for inhibiting RAF-kinase in a human or mammal generally’. The guidance in the specification is limited to an *in vitro* cell proliferation assay showing inhibition of two colon cancer cell lines; and summary instructions relating to an *in vivo* assay in mice that can be performed to determine the inhibition of a human adenocarcinoma cell line (see pages 34-35).

Applicant argues that ‘no evidence has been presented to refute the findings or conclusions made in the publications’. However, contrary to applicant’s arguments, the state of the art references Kolch and/or Monia do not establish a therapeutic method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas generally. As explained in the previous office action, the state of the art is not indicative of the fact that treatment of all

Art Unit: 1624

types of diseases encompassed by the instant claims are conventional or well known. The cited references are too speculative and invite further research into treatment of cancer diseases. For example, Monia at page 668 provides that “the emergence of novel therapies that specifically reverse the oncogenic effect of these gene products has generally been slow”.

Next, applicant draws attention to references cited in Information Disclosure Statements filed May 29, 2007. However, many of these references are published after the filing date of the instant application and are not therefore, state of the art references as of the filing date. Further, the Cecil reference (1996, previously cited) establishes that – “clinical and laboratory observations have provided a reasonable framework. This framework should be used with caution, however, because it is certain that the intrinsic factors that control tumor growth and propagation are far more complex, episodic and heterogeneous than we know, even within a single tumor mass” (see page 1004). Thus, contrary to applicant’s arguments, the state of the art as of the filing date of the application, does not establish that a single therapeutic approach exists for the treatment of the types of diseases within the scope of instant claims.

Further, claim 117 is directed towards ‘a method for inhibiting RAF-kinase in a human or mammal’ and therefore reaches through to the treatment of all types of diseases associated with RAF-kinase. The findings and conclusions in the cited publications are with respect to inhibition of RAF kinase and the application of such activity for specific types of cancerous growth. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth

Art Unit: 1624

control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The evidence of record does not disclose any known compounds of similar structure, which have been demonstrated to inhibit RAF-kinase generally and thereby treat all diseases mediated by raf kinase; or treat all types of solid tumors, carcinomas, myeloid disorders or adenomas, when the compounds are administered to a human or a mammal.

2. Claims 74, 81, 87, 93, 99-104, 106-115 and 117-119 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38, 89-91, 121 of copending Application No. 10/042,226. The copending application contains claims drawn to a genus, as well as the species (see e.g., claim 121 of 10/042,226) of the instant claims used in 'a method for the treatment of cancerous cell growth mediated by raf kinase' and the specification of application provides that such diseases include, for example, solid cancers, etc. (see page 2).

Receipt is acknowledged of the Information Disclosure Statements filed on May 11, May 29 and June 29, 2007 and copies are enclosed herewith.

Art Unit: 1624

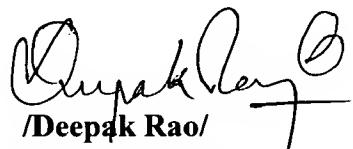
***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
/Deepak Rao/  
Primary Examiner  
Art Unit 1624

September 17, 2007